

APPENDIX A

1. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4
5 comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D-E, wherein

10 A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

15 C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes an immunoglobulin constant region-like domain,

D comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a transmembrane domain, and

20 E comprises a nucleotide sequence of at least one fifth exon of a T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a cytoplasmic domain,

25 with the proviso that E is not any of the following nucleotide sequences selected from a group consisting of SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29 and SEQ ID NO:31.

2. The isolated nucleic acid of claim 1 which is a cDNA.

30 3. The isolated nucleic acid of claim 2 which comprises a coding region of the cDNA.

4. The isolated nucleic acid of claim 1, wherein the nucleotide sequence is derived from a T cell costimulatory molecule gene encoding B7-1.

35 5. The isolated nucleic acid of claim 4, wherein B7-1 is murine.

6. The isolated nucleic acid of claim 4, wherein B7-1 is human.

5

7. The isolated nucleic acid of claim 5, wherein E comprises a nucleotide sequence shown in SEQ ID NO:4.

8. The isolated nucleic acid of claim 5, wherein E comprises a nucleotide sequence encoding an amino acid sequence shown in SEQ ID NO:5.

9. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 and is encoded by a T cell costimulatory molecule gene having

15 at least one first exon encoding a first cytoplasmic domain comprising a nucleotide sequence selected from the group consisting of a nucleotide sequence of SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29 and SEQ ID NO:31, and

at least one second exon encoding a second cytoplasmic domain, wherein the isolated nucleic acid comprises a nucleotide sequence encoding the second cytoplasmic domain.

20

10. The isolated nucleic acid of claim 9 which comprises a coding region of a cDNA.

11. The isolated nucleic acid of claim 9 which does not comprise a nucleotide sequence encoding the first cytoplasmic domain.

12. The isolated nucleic acid of claim 9 wherein the T cell costimulatory molecule gene is B7-1.

30

13. The isolated nucleic acid of claim 12 wherein B7-1 is murine.

14. The isolated nucleic acid of claim 12 wherein B7-1 is human.

15. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 35 comprising a nucleotide sequence shown in SEQ ID NO:1.

16. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a nucleotide sequence shown in SEQ ID NO:3.

5 17. An isolated nucleic acid encoding a cytoplasmic domain derived from a protein which binds CD28 or CTLA4, the nucleic acid comprising a nucleotide sequence shown in SEQ ID NO:4.

10 30. A recombinant expression vector comprising the nucleic acid molecule of claim 15.

31. A host cell which contains the recombinant expression vector of claim 30.

15 33. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D-E, wherein

20 A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

25 C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes an immunoglobulin constant region-like domain,

D, which may or may not be present, comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a transmembrane domain, and

30 E, which may or may not be present, comprises a nucleotide sequence of at least one fifth exon of a T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a cytoplasmic domain,

with the proviso that A is not any of the following nucleotide sequences selected from a group consisting of SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39 and SEQ ID NO:41.

- 5 34. The isolated nucleic acid of claim 33 which is a cDNA.
35. The isolated nucleic acid of claim 34 which comprises a coding region of the cDNA.
- 10 36. The isolated nucleic acid of claim 33, wherein the nucleotide sequence is derived from a T cell costimulatory molecule gene encoding B7-2.
37. The isolated nucleic acid of claim 36, wherein B7-2 is murine.
- 15 38. The isolated nucleic acid of claim 36, wherein B7-2 is human.
39. The isolated nucleic acid of claim 37, wherein A comprises a nucleotide sequence shown in SEQ ID NO:14.
- 20 40. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 and is encoded by a T cell costimulatory molecule gene having at least one first exon encoding a first signal peptide domain comprising a nucleotide sequence selected from the group consisting of a nucleotide sequence of SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37 SEQ ID NO:39 and SEQ ID NO:41, and
- 25 at least one second exon encoding a second signal peptide domain, wherein the isolated nucleic acid comprises a nucleotide sequence encoding the second signal peptide domain.
41. The isolated nucleic acid of claim 40 which comprises a coding region of a cDNA.
- 30 42. An isolated nucleic acid which encodes a protein which binds to CD28 or CTLA4, wherein said nucleic acid molecule comprises a nucleotide sequence shown in SEQ ID NOs: 4 and 14.

43. The isolated nucleic acid of claim 40 wherein the T cell costimulatory molecule gene is B7-2.

44. The isolated nucleic acid of claim 43 wherein B7-2 is murine.

5

45. The isolated nucleic acid of claim 43 wherein B7-2 is human.

10 46. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a nucleotide sequence shown in SEQ ID NO:12.

15 47. An isolated nucleic acid encoding a signal peptide domain derived from a protein which binds CD28 or CTLA4, the nucleic acid comprising a nucleotide sequence shown in SEQ ID NO:14.

60. A recombinant expression vector comprising the nucleic acid molecule of claim 46.

20 61. A host cell which contains the recombinant expression vector of claim 60.

63. An isolated nucleic acid encoding a protein comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D, wherein

25

A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

30 B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin constant region-like domain,

C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes a transmembrane domain, and

D comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a cytoplasmic domain.

5 64. The isolated nucleic acid of claim 63 comprising a nucleotide sequence shown in SEQ ID NO:8.

65. The isolated nucleic acid of claim 63 comprising a nucleotide sequence shown in SEQ ID NO:10.

10 69. An isolated nucleic acid encoding a protein comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D, wherein

15 A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

20 B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes a transmembrane domain, and

25 D comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a cytoplasmic domain.

70. The isolated nucleic acid of claim 69 comprising a nucleotide sequence shown in SEQ ID NO:62.

30 71. The isolated nucleic acid of claim 69 comprising a nucleotide sequence shown in SEQ ID NO:64.

75. A recombinant expression vector comprising the nucleic acid molecule of
35 claim 69.

76. A host cell which contains the recombinant expression vector of claim 75.

77. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4
5 comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D-E, wherein:

10 A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

15 C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes an immunoglobulin constant region-like domain,

D comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a transmembrane domain, and

20 E comprises a nucleotide sequence of at least one fifth exon of a T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a cytoplasmic domain,

25 with the proviso that E is not any of the following nucleotide sequences selected from a group consisting of SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29 and SEQ ID NO:31; or wherein

30 A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes an immunoglobulin constant region-like domain,

5 D, which may or may not be present, comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a transmembrane domain, and

E, which may or may not be present, comprises a nucleotide sequence of at least one fifth exon of a T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a cytoplasmic domain,

10

with the proviso that A is not any of the following nucleotide sequences selected from a group consisting of SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39 and SEQ ID NO:41.